Delivery of the biologically active compounds to the cell cytoplasm is facilitated by co-endocytosis of the biologically active compounds with the maleic anhydride-containing polymers ~~for delivery of the~~. In one aspect of the invention, the biologically active compound and the maleic anhydride-containing polymers are not associated with each other but are both endocytosed by the cell. In another aspect of the invention, the biologically active compound and the maleic anhydride-containing polymer are associated with each other via covalent or non-covalent interactions. Non-covalent interactions include ionic interactions, hydrophobic interactions, Van der Waals interactions, and affinity interactions. This association can enable or enhance co-endocytosis of the biologically active compound and the maleic anhydride-containing polymers. The cell can be in vitro or in vivo. For delivery of a biologically active compound to a cell in vivo, the polymer and biologically active compound are inserted into the animal is a manner that permits the polymer and the biologically active compound to come into contact with the cell. Parenteral routes of administration include intravascular, intramuscular, intraparenchymal, intradermal, subdermal, subcutaneous, intratumor, intraperitoneal, intrathecal, subdural, epidural, and intralymphatic injections that use a syringe and a needle or catheter. Other routes of administration include intraparenchymal into tissues such as muscle (intramuscular), liver, brain, and kidney. Epithelial routes include oral, nasal, respiratory, and vaginal routes of administration.

Example 1. Drug delivery to cells using anionic maleic anhydride-based polymers: To assess the ability of these polymers to aid in the delivery of a biologically active compound we chose to assess the ability of these polymers to ~~delivery~~ deliver an antisense oligonucleotide.

To ~~delivery~~ deliver anionic oligos, cationic lipids [Hope et al. 1998; Audouy et al. 2001] and polymers [Robaczewska et al. 2001] that are effective at plasmid DNA delivery are commonly used. However, in order to use these strategies for the delivery of uncharged oligonucleotides such as PMO's, the PMO must first be complexed with a complimentary strand of anionic oligonucleotide to form a charged complex. Two other methods for delivering PMOs, scrape-loading and syringe-loading, both involve physically damaging cells to create transient lesions in the plasma membrane [Ghosh et al. 2000].

Example 8. Morpholino Delivery Assay: HeLa Tet-Off cells (Clontech Laboratories, Palo Alto, CA) were grown in Delbecco's Modified Eagle's Medium (DMEM, Cellgro, Herndon, VA) containing 10% fetal bovine serum (FBS) (Hyclone Laboratories, Logan, Utah) in a humidified incubator at 37°C with 5% CO2 atmosphere. The cells were plated in 24-well culture dishes at a density of 3 x 106 cells/well and incubated for 24 hours. Medium was replaced with 0.5 ml DMEM, with or without 10% FBS, containing 0.5 µmol morpholino (CCT CTT ACC TCA GTT ACA ATT TAT A, SEQ ID NO: 1 ~~SEQ ID 10~~, Gene Tools, Philomath, OR) and either containing or not containing 20 µg of various polyanions. The cells were incubated for 4 hours in a humidified, 5% CO2 incubator at 37°C. The media was then replaced with Dubelco's modified Eagle Media containing10% fetal bovine serum. The cells were then incubated for 48 h. The cells were then harvested and the lysate was then assayed for luciferase expression as previously reported [Wolff et al. 1990]. A Lumat LB 9507 (EG&G Berthold, Bad-Wildbad, Germany) luminometer was used. The amount of luciferase produced in the presence of morpholino and polyanion was normalized to the amount produced in the absence of polyanion and reported in Table 1.